INTERSPECIES EMBRYONIC STEM CELL

CLAIMS

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1. An isolated embryonic stem cell (ES), characterised in that it is an interspecies Mus musculus X Mus spretus hybrid ES cell.

2. The ES cell of any of claim 1, characterised in that said interspecies hybrid stem cells
10   have germ line transmission capability.

3. The interspecies Mus musculus x Mus spretus ES cell lines of claim 1 or 2, characterised in that more than 40% of the microsatellites of its DNA are polymorphic in length.

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4. The interspecies Mus musculus x Mus spretus ES cell lines of claim 1 or 2, characterised in that more than 70% of the microsatellites of its DNA are polymorphic in length.

20 5. The interspecies Mus musculus x Mus spretus ES cell lines of claim 1 or 2, characterised in that more than 90% of the microsatellites of its DNA are polymorphic in length.

6. The ES cell as in the claims 1or 5, wherein the Mus spretus genomic background is
25   from SPRET/Ei (Spain) Ei Mus spretus strain mice.

7. The ES cell as in the claims 1or 5, wherein the Mus musculus genomic background is from C57BL/6J

30 8. The ES cell as in the claims 1or 7, characterised in that the interspecies hybrid ES cell are derived from SPRET/Ei Mus spretus strain x C57BL6/J Mus musculus strain.

9. A population of the isolated embryonic stem cell (ES) of the claims 1 to 8.

35 10. A pure population of the isolated embryonic stem cell (ES) of the claims 1 to 8.

11. The use of the interspecies Mus musculus x Mus spretus hybrid ES cells of the claims 1 to 10 in a method for introducing mutations into the Mus spretus genome.

40 12. The use of the interspecies Mus musculus x Mus spretus hybrid ES cells of the claims 1 to 10 in a method for introducing mutations specifically into Mus spretus allele.

13. The use of the the interspecies Mus musculus x Mus spretus hybrid ES cells of the claims 1 to 10 in a method for introducing mutations into the Mus spretus genome,

said method comprising a) transfection of the interspecies Mus musculus x Mus spretus hybrid embryonic stem (ES) cells with a gene-targeting construct, which specifically recombines homologously with the Mus spretus gene, b) assessing Mus musculus x Mus spretus hybrid ES cells for homologous recombination, c) generating chimeric mice by blastocyst injection d) assessing germline transmission of the Mus spretus genome and e) breeding the chimeric mice, which transmit the Mus spretus genome, to homozygosity, in a pure Mus spretus background.

14. The use of claims 11 to 13, wherein the mutations are of the groups consisting of, null mutations, point mutations, translocations, inversions or deletions.

15. The use of the interspecies Mus musculus x Mus spretus hybrid ES cells of the claims 1 to 10 in a method for analysing gene function or identification of quantitative trait loci comprising the generation of radiation induced chromosomal deletion in high polymorphism interspecies hybrid ES cells of Mus musculus x Mus spretus of the claim 1 to 10.

16. A method for introducing mutations into the Mus spretus genome, comprising a) transfection of the interspecies Mus musculus x Mus spretus hybrid embryonic stem (ES) cells with a gene-targeting construct, which specifically recombines homologously with the Mus spretus gene, b) assessing Mus musculus x Mus spretus hybrid ES cells for homologous recombination, c) generating chimeric mice by blastocyst injection, d) assessing germline transmission of the Mus spretus genome and e) breeding the chimeric mice, which transmit the Mus spretus genome, to homozygosity, in a pure Mus spretus background.

17. The method of claim 16, wherein the mutations are of the groups consisting of, null mutations, point mutations, translocations, inversions or deletions.

18. A method for analysing gene function or identification of quantitative trait loci comprising the generation of radiation induced chromosomal deletion in the interspecies hybrid ES cells of Mus musculus x Mus spretus of claim 1 to 10.

19. An high-through put analysis system comprising the cell or cell population of any of the claims 1 to 10, for analysing gene function

20. An high-through put analysis system comprising the cell or cell population of any of the claims 1 to 10, for analysing gene function for identification of quantitative trait loci